

Ivan PETYAEV  
Appl. No. 10/574,852  
Atty. Ref.: 620-433  
Amendment After Final Rejection  
December 16, 2008

REMARKS

Reconsideration is requested.

Claims 12, 13, 14, 16-22 and 29-32 are pending.

Claims 14, 16-20, 30 and 31, have been canceled, without prejudice, and claims 33 and 34 added above. Claims 12, 13, 21, 22, 29 and 32-34 will be pending upon entry of the present Amendment.

The claims have been amended, without prejudice, to advance prosecution.

Claim 12 has been revised, without prejudice, to define a method of previously-considered claims 31 and 32 wherein the metal chelator is further defined as recited in previously-considered claim 20 and the anti-microbial agent is as described in previously-considered claim 18. Claims 21 and 22 have been revised to be consistent with the revisions to claim 12. Claim 32 has been further revised, without prejudice, to further define the anti-microbial agent and metal chelator. New claims 33 and 34 have been added to define the further step of the method of claim 12 which is similar to claim 32. The claim amendments are not believed to raise new issues requiring further search and/or consideration. No new matter has been added. New claims have not been added without canceling a corresponding number of claims. Entry of the present Amendment is requested.

The Section 103 rejection of claims 12-14, 16-22, 27 and 29-32 over Petyaev (WO 03/017992) and Shiff (U.S. Patent No. 6,201,028) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

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The Examiner confirms that Petyaev does not disclose the treatment of hyperlipidemia. See page 2 of the Office Action dated October 8, 2008. The Examiner asserts that Schiff discloses that hyperlipidemia is associated with atherosclerosis, which would have allegedly provided motivation for one of ordinary skill in the art to have used compositions of Petyaev to treat hyperlipidemia with a reasonable expectation of success.

The applicants submit however that the results set out in Schiff indicate that aspirin lowered plasma cholesterol levels (Table 1) and inhibited atherogenesis (Table 2) relative to controls, although this effect was not statistically significant (col. 11, line 15). Schiff further states at col. 8, lines 19-23 that;

"... aspirin and sulindac and NSAIDs in general are useful for the prevention and treatment of hyperlipidemia and atherosclerosis".

However, Schiff is devoid of any teaching regarding the effect of aspirin on LDL-cholesterol or its components.

From the disclosure of Schiff, a person of ordinary skill in the art would not have reasonably expected that aspirin in combination with azithromycin would have affected apolipoprotein-B and LDL-cholesterol levels in hyperlipidemia patients. The applicants note that the teaching of Schiff is limited to the administration of aspirin alone. The evidence of the present specification demonstrates that aspirin alone does not reduce apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels. Aspirin has this effect only when combined with azithromycin ("Group B"). There is

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neither a teaching nor a suggestion in Shiff to combine aspirin with azithromycin or to have looked to Petyaev to have made the presently claimed invention.

There was no suggestion in either Shiff or Petyaev that would have led one of ordinary skill in the art to have reasonably predicted that apolipoprotein-B levels in the vascular system might be reduced without causing a concomitant reduction LDL-cholesterol levels. This technical effect of the presently claimed invention was entirely unexpected.

The disclosure of Shiff would therefore not have led a person of ordinary skill in the art to have expected that the compositions which are disclosed by Petyaev could have been used to alter the levels of apolipoprotein-B in the vascular system without reducing LDL-cholesterol levels in an individual having hyperlipidemia, as claimed.

Withdrawal of the Section 103 rejection of claims 12-14, 16-22, 27 and 29-32 over Petyaev (WO03/017992) in view of Shiff et al (U.S. Patent No. 6,201,028) is requested.

The Section 103 rejection of claims 12-14, 16-22 and 29-32 over Klein (U.S. Patent No. 6,174,865) and Shiff (U.S. Patent No. 6,201,028) is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following distinguishing comments.

The Examiner is understood to believe that it would have been *prima facie* obvious to have used a combination of a macrolide antibiotic with aspirin for the treatment of hyperlipidemia because, allegedly, a person of ordinary skill in the art

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would have expected the results of such a combination from the teachings of Klein combined with the teachings of Schiff.

The applicants understand Klein to teach that erythromycin compounds such as clarithromycin reduce triglyceride levels in patients diagnosed with hypertriglyceridemia. LDL and cholesterol levels remain on or above baseline levels during this treatment (see Figures 1 and 2). Klein therefore teaches that erythromycin compounds reduce triglyceride levels but have little or no effect on LDL in patients.

From the disclosure of Klein, a person of ordinary skill in the art would not have reasonably expected that azithromycin in combination with aspirin could have been used to alter the levels of apolipoprotein-B in the vascular system without reducing LDL-cholesterol levels in an individual having hyperlipidemia, as claimed.

The applicants believe Klein is limited to the administration of erythromycin compounds alone. The evidence of the present specification demonstrates that azithromycin alone does not reduce apolipoprotein-B levels in the vascular system without reducing LDL-cholesterol levels. Azithromycin has this effect only when combined with aspirin ("Group B"). There is neither a teaching nor a suggestion in Klein or Schiff to have combined azithromycin with aspirin, to have made the presently claimed invention.

Furthermore, there is no suggestion in either Klein or Schiff that apolipoprotein-B levels in the vascular system might be reduced without causing a concomitant reduction LDL-cholesterol levels. This technical effect of the presently claimed invention was entirely unexpected.

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A person of ordinary skill would not have expected from the cited art that a combination of azithromycin and aspirin could be successfully used to alter the levels of apolipoprotein-B in the vascular system without reducing LDL-cholesterol levels in an individual having hyperlipidemia, as claimed.

Withdrawal of the Section 103 rejection of claims 12-14, 16-22 and 29-32 over Klein and Shiff et al is requested.

The claims are submitted to be in condition for allowance and entry of the present Amendment and a Notice of Allowance are requested. The Examiner is requested to contact the undersigned, preferably by telephone, in the event anything further is required.

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

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